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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/693,480	10/23/2003	Silviu Itescu	0575/66602-B/JPW/BJA	2572

23432 7590 09/15/2011

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EXAMINER	
BUNNER, BRIDGET E	

ART UNIT	PAPER NUMBER
1647	

MAIL DATE	DELIVERY MODE
09/15/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/693,480	ITESCU, SILVIU	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 July 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *35,37,43,46,47,49-51 and 57* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *35,37,43,46,47,49-51 and 57* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☒ The drawing(s) filed on *01 February 2008 and 23 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/18/11*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 18 July 2011 has been entered.

Status of Application, Amendments and/or Claims

Claims 35, 37, 43, 46, 47, 49-51 and 57 are under consideration in the instant application.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 18 July 2011 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. It is noted that the citation for patent 7,662,392 has been crossed off of the IDS because this patent was previously cited on the PTO-892 form of 18 January 2011.

Withdrawn Objections and/or Rejections

1. The rejection of claims 35, 37, 43, and 57 under 35 U.S.C. § 103(a) as being unpatentable over Peterson, BE (US 2002/0094327) and Hung et al. (US 2003/0171294) as set forth at pages 5-10 of the previous Office Action (18 January 2011) is *withdrawn* because Peterson and Hung et al. do not teach treating a subject suffering from a disorder of a heart tissue involving loss or apoptosis of cardiomyocytes.

2. The rejection of claim 47 under 35 U.S.C. § 103(a) as being unpatentable over Peterson, BE (US 2002/0094327) and Hung et al. (US 2003/0171294) as applied to claims 35, 37, 43, 46, 57, and further in view of Rempel et al. (Clin Can Res 6: 102-111, 2000) as set forth at pages 10-12 of the previous Office Action (18 January 2011) is *withdrawn* because Peterson and Hung et al. do not teach treating a subject suffering from a disorder of a heart tissue involving loss or apoptosis of cardiomyocytes.

3. The rejection of claims 49-51 under 35 U.S.C. § 103(a) as being unpatentable over Peterson, BE (US 2002/0094327) and Hung et al. (US 2003/0171294) as applied to claims 35, 37, 43, 46, and 57, further in view of Isner et al. (WO 99/45775) as set forth at pages 12-13 of the previous Office Action (18 January 2011) is *withdrawn* after further consideration by the Examiner.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 35, 37, 43, 46-47, 49, 50, 51 and 57 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 7,662,392. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to a method of treating a disorder of the heart comprising administering stromal-derived factor-1. The basis for this rejection is set forth at pages 2-5 of the previous Office Action of 18 January 2011, pages 2-3 of the Office Action of 18 September 2009, pages 2-3 of the Office Action of 03 February 2009, page 4 of the Office Action of 09 May 2008 and pages 6-7 of the Office Action of 08 August 2007.

At page 4 of the Response of 18 July 2011, Applicant argues that the subject application teaches that there are two distinct methods for administering SDF-1 to improve cardiac function. Applicant asserts that the pending claims recite a method of treating a disorder of a heart tissue involving loss or apoptosis of cardiomyocytes by inducing regeneration of endogenous cardiomyocytes, while the '392 patent claims are directed to a method of increasing trafficking of bone-marrow derived endothelial progenitor cells to ischemic myocardium. Applicant submits that the claimed method directed to induce regeneration of endogenous cardiomyocytes is not

obvious over a method of increasing trafficking of bone-marrow-derived endothelial progenitor cells to ischemic myocardium.

Applicant's arguments have been fully considered but are not found to be persuasive. As discussed in the previous Office Action of 18 January 2011, claim 35 of the instant application recites intramyocardial or intracoronary administration of SDF-1α or SDF-1β to a subject suffering from a disorder of heart tissue involving loss or apoptosis of cardiomyocytes. Claim 1 of the '392 patent recites administering SDF-1 to a subject effective to attract bone marrow-derived endothelial progenitor cells to the ischemic myocardium so as to thereby increase trafficking of bone marrow-derived endothelial progenitor cells to the ischemic myocardium, and wherein the SDF-1 is administered to the subject by injection into the heart muscle. Claims 35, 46, and 47 of the instant application and claims 2-3 of the '392 patent recite that the SDF-1 is SDF-1α or SDF-1β. Claim 49 of the instant application recites that the disorder of the heart comprises myocardial infarction, congestive heart failure, chronic ischemia, ischemic disease, diabetic heart disease or cardiomyopathy. Claim 5 of the '392 patent recites that the subject has suffered or is suffering from myocardial infarction, chronic heart failure, ischemic heart disease, coronary artery disease, diabetic heart disease, hemorrhagic stroke, thrombotic stroke, or other diseases in which the myocardium is rendered ischemic.

Hence, both the claims of the instant application and the claims of the '392 patent recite administration of SDF-1 to the same subject population (subjects suffering myocardial infarction, ischemic heart disease, or diabetic heart disease) and to the same tissue (i.e., heart muscle (myocardium)). A compound and all of its properties are inseparable; they are one and the same thing and simply stating a new property of SDF-1 does not render the claimed method of the

instant application unobvious over the claims of the '392 patent (see *In re Papesch*, CCPA 137 USPQ 43; *In re Swinehart and Sfiligoj*, 169 USPQ 226 (CCPA 1971); *In re May*, 574 F.2d 1082, 1090, 197 USPQ 601, 607 (CCPA 1978)).

5. Claims 35, 37, 43, 46-47, 49-51, and 57 69, 70, 72-79 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 69, 70, 72-75, 77-78 of copending Application No. 12/657,264. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to a method of administering stromal-derived factor-1.

Claim 35 of the instant application is directed to a method of treating a subject suffering from a disorder of a heart tissue involving loss or apoptosis of cardiomyocytes comprising intramyocardially or intracoronarily administering to the subject human stromal derived factor-1, wherein the human stromal derived factor-1 is human stromal-derived factor-1α or stromal-derived factor-1β. Claim 69 of the '264 application recites a method of increasing trafficking of endothelial progenitor cells to an ischemic myocardium in a subject's heart comprising administering to the subject's heart an amount of stromal derived factor-1 (SDF-1). Claims 74 and 75 of '264 further recite that the SDF-1 is SDF-1α and SDF-1β. Both sets of claims recite that the tissue is heart tissue and that the SDF-1 is administered into the heart. Both sets of claims also recite that the disorder or subject who is suffering has a myocardial infarction. It is noted that a compound and all of its properties are inseparable; they are one and the same thing (see *In re Papesch*, CCPA 137 USPQ 43; *In re Swinehart and Sfiligoj*, 169 USPQ 226 (CCPA 1971); *In re May*, 574 F.2d 1082, 1090, 197 USPQ 601, 607 (CCPA 1978)).

Thus, the instant claims are not patentably distinct over the co-pending claims in Application No. 12/657,264.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 35, 37, 43, 46, 47, 49-51, and 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Isner et al. (WO 99/45775), Watanabe et al. (Basic Res Cardiol 93: 30-37, 1998) and Rempel et al. (Clin Can Res 6: 102-111, 2000).

Isner et al. teach a methods for inducing angiogenesis in ischemic tissue of patient in need of such treatment by administration of a vascularization modulating agent (page 14, lines 18-21). Isner et al. teach that the vascularization modulating agent may be SDF-1 (page 21, lines 13-18). Isner et al. continue to disclose that method of the invention may be used to prevent or treat ischemic cardiomyopathy, cerebrovascular ischemia, and myocardial ischemia (page 15, lines 1-5). It is well known in the art that there is a loss or apoptosis of cardiomyocytes in acute myocardial ischemic injury as evidenced by Buja et al. (Cardiovasc Pathol 17(6): 349-374, 2008;; see pages 358-362; Figure 3). Isner et al. teach that ischemia may adversely impact heart

or brain tissue (page 15, lines 8-10). Isner et al. also state that administration of the agent may be intramuscular (page 18, line 19).

Isner et al. do not teach that SDF-1 is human SDF-1α or human SDF-1β. Isner et al. also do not teach intramyocardial or intracoronary administration of SDF-1

Rempel et al. teaches that the human SDF-1 gene encodes two isoforms, SDF-1α and SDF-1β, that arise from alternative splicing (page 102, column 2, last paragraph; page 103, column 1). Rempel et al. also disclose that these isoforms differ only in that SDF-1β contains four additional 3' amino acids (page 102, column 2, last paragraph).

Watanabe et al. teach that administration of growth factors is emerging as a new therapeutic approach for the enhancement of collateral vessel formation in the ischemic heart (abstract). Watanabe et al. disclose that the growth factor, FGF-2 (or bFGF), is injected alone or with heparin or heparan sulfate into normal myocardium and the border zone of ischemic myocardium in a porcine myocardial infarct model (page 31, column 1, middle of second paragraph; abstract; Figure 1). Watanabe et al. disclose that delivery of FGF-2 increases the density of arterioles in normal myocardium and the border zone area (page 34; page 35, top of column 1). Specifically, Watanabe et al. teach that in the ischemic border zone area, an increase in the density of arterioles is observed in the FGF-2 alone group, FGF-2 plus heparin, and FGF-2-coated heparin bead groups as compared with control (page 35, top of column 1; see also Figures 4A and 4B). Watanabe et al. conclude that induction of collateral vessels in the compromised areas may improve the clinical course of ischemic heart disease (page 36, column 2, last paragraph).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the method of administering of SDF-1 to a subject suffering from ischemic cardiomyopathy, cerebrovascular ischemia, and myocardial ischemia as taught by Isner et al. by intramyocardially administering human SDF-1α or SDF-1β as taught by Rempel et al. and Watanabe et al. The person of ordinary skill in the art would have been motivated to make that modification in order to localize angiogenesis or induction of collateral vessels to the ischemic heart of the patient. The person of ordinary skill in the art reasonably would have expected success because (i) similar angiogenic growth factors were already being intramyocardially administered to the heart at the time the invention was made and (ii) SDF-1α and SDF-1β are isoforms encoded from the SDF-1 gene. Therefore, the claimed invention as a whole was clearly *prima facie* obvious over the prior art.

Since Isner et al. (in combination with Watanabe et al. and Rempel et al.) teach the administration of SDF-1 to the same subject population and to the same tissue as recited in the claims, the regeneration of endogenous cardiomyocytes must have been inherently occurring in the prior art. The disclosure of Isner et al. (in combination with Watanabe et al. and Rempel et al.) meets the terms of the claimed method because SDF-1 inherently possesses endogenous cardiomyocyte regeneration activity, absent evidence to the contrary (*In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977)). A compound and all of its properties are inseparable; they are one and the same thing and simply stating a new property of SDF-1 does not render the claimed method of the instant application free of the art (see *In re Papesch*, CCPA 137 USPQ 43; *In re Swinehart and Sfiligoj*, 169 USPQ 226 (CCPA 1971); *In re May*, 574 F.2d 1082, 1090, 197 USPQ 601, 607 (CCPA 1978)). Furthermore, inherent anticipation does not require that one

of ordinary skill in the art recognize an inherent feature in a prior art disclosure (*Schering Corp. v. Geneva Pharmaceuticals Inc.*, 67 USPQ2d 1664 (CAFC 2003); *Toro Co. v. Deere & Co.*, 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004)).

Conclusion

No claims are allowable.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

Stegman et al. Therapeutic angiogenesis: intramyocardial growth factor delivery of FGF-1 as sole therapy in patients with chronic coronary artery disease. Cardiac Vascul Regen 1: 259-267, 2000.

Freedman et al. Ann Internal Med 136: 54-71, Jan 2002 (review of therapeutic angiogenesis for coronary artery disease; see Tables 2-3)

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571)272-0881. The examiner can normally be reached on 9:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BEB
Art Unit 1647
06 September 2011

/Bridget E Bunner/
Primary Examiner, Art Unit 1647